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ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,
SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA,
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Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted
a patent (Rule 4.17(ii)) for the following designations AE,
AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,
CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE,
EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN,
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MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
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ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD,
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KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG,
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT,
LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ,
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- of inventorship (Rule 4.17(iv)) for US only

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For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: MODULATION OF ACTIVITY OF NEUROTROPHINS

(57) Abstract: The present invention relates to methods for modulating the activity of one or more neurotrophins, such as neural growth factor (NGF), brain derived neurotrophic factor (BDNF), neurotrophin-3, and neurotrophin-4 (NT-4), in an animal and methods for treatment of a disease or disorder in an individual by modulation of neurotrophin activity. The modulation is carried out by interfering with binding between a neurotrophin and a receptor of the Vps10p-domain receptor family or modulating the expression of a receptor of the Vps10p-domain receptor family. Methods for screening for agents capable of modulating neurotrophin activity and agents selected using these screening methods are also disclosed, as are methods for determining the effect of an agent on one or more neurotrophins in cells. The present invention also pertains to methods for modulating the transport of one or more neurotrophins.

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/DK 03/00919

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K38/18 A61K39/395 G01N33/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, EPO-Internal, MEDLINE, WPI Data, PAJ.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	FAHNESTOCK MARGARET ET AL: "The precursor pro-nerve growth factor is the predominant form of nerve growth factor in brain and is increased in Alzheimer's disease" MOLECULAR AND CELLULAR NEUROSCIENCE, vol. 18, no. 2, August 2001 (2001-08), pages 210-220, XP002294169 ISSN: 1044-7431 abstract	1-57
A	US 2001/046956 A1 (HADCOCK JOHN R) 29 November 2001 (2001-11-29) claims --- -/-	1-57

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/DK 03/00919

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PETERSEN C MUNCK ET AL: "Propeptide cleavage conditions sortilin/neurotensin receptor-3 for ligand binding" EMBO (EUROPEAN MOLECULAR BIOLOGY ORGANIZATION) JOURNAL, vol. 18, no. 3, 1 February 1999 (1999-02-01), pages 595-604, XP002294170 ISSN: 0261-4189 page 595, column 1 -page 596, column 1, paragraph 1	54
A	---	1-53, 55-57
X	JACOBSEN L ET AL: "Activation and functional characterization of the mosaic receptor SorLA/LR11." THE JOURNAL OF BIOLOGICAL CHEMISTRY. UNITED STATES 22 JUN 2001, vol. 276, no. 25, 22 June 2001 (2001-06-22), pages 22788-22796, XP002294171 ISSN: 0021-9258 abstract	54
A	---	1-53, 55-57
X	MAZELLA J ET AL: "The 100-kDa neurotensin receptor is gp95/sortilin, a non-G-protein-coupled receptor." THE JOURNAL OF BIOLOGICAL CHEMISTRY. UNITED STATES 9 OCT 1998, vol. 273, no. 41, 9 October 1998 (1998-10-09), pages 26273-26276, XP002294172 ISSN: 0021-9258 abstract	54
X	HAMPE WOLFGANG ET AL: "The genes for the human VPS10 domain-containing receptors are large and contain many small exons" HUMAN GENETICS, vol. 108, no. 6, June 2001 (2001-06), pages 529-536, XP002294173 ISSN: 0340-6717 page 529, column 1 -page 530, column 1, paragraph 1 -----	54

INTERNATIONAL SEARCH REPORT

International application No.
PCT/DK 03/00919

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: Claims: 1-30, 41-43, 45-50 (entirely), 32-39 (partially)
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☒ Claims Nos.: Claims: 1-15, 44-49 (entirely), 25-30, 50 (partially)
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Claims Nos.: Claims: 1-30, 41-43, 45-50 (entirely), 32-39 (partially)

Claims 1-30, 41-43, 45-50 (entirely), 32-39 (partially; probably due to an incorrect reference to claim 30) relate to methods of treatment of the human or animal body by surgery or by therapy or diagnostic methods practised on the human or animal body (PCT Rule 39.1(iv)). Nevertheless, a search has been executed for these claims. The search has been based on the alleged effects of the compounds or compositions (see further Box II.2).

Continuation of Box I.2

Claims Nos.: Claims: 1-15, 44-49 (entirely), 25-30, 50 (partially)

Present claims 1-15, 44-49 (entirely) and claims 25-30, 50 (partially) relate to an extremely large number of possible agents. Support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the agents claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.

Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts related to the agents which have been specified in claims 16-19, 21-24.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

In: Application No

PCT/DK 03/00919

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2001046956	A1	29-11-2001	
		AU 3888801 A	01-11-2001
		CA 2345180 A1	27-10-2001
		EP 1157695 A1	28-11-2001
		HU 0101666 A2	28-02-2002
		JP 2002275092 A	25-09-2002
		NZ 511354 A	28-03-2003
		ZA 200103365 A	25-10-2002
